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$$CH_3 = 0 \longrightarrow_{\mathbf{n}} 0 \xrightarrow{\mathbf{N}}_{\mathbf{H}} \underbrace{\mathbf{R}_1}_{\mathbf{R}_2} \mathbf{S} - \mathbf{S}$$

$$0 \longrightarrow_{\mathbf{n}} \mathbf{N} \longrightarrow_{\mathbf{H}} \mathbf{Ligand}$$

Fig. 1A

$$CH_{3} = O \longrightarrow_{n} O \longrightarrow_{H} R_{1} R_{2}$$

$$R' = SH$$

$$CH_{3} = O \longrightarrow_{n} O \longrightarrow_{H} R_{1} R_{2}$$

$$S = CH_{3} + CO_{2} + H_{2}N \longrightarrow_{Ligand}$$

Fig. 1B

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Fig. 2

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Fig. 3A

$$CH_{3} = 0 \longrightarrow_{n} 0 \longrightarrow_{H} 0 \longrightarrow_{R} S \longrightarrow_{R} 0 \longrightarrow_{H} 0 \longrightarrow_{H} 1 \text{ Lipid}$$

$$CH_{3} = 0 \longrightarrow_{n} 0 \longrightarrow_{H} 0 \longrightarrow_{R} S \longrightarrow_{S} R \longrightarrow_{H} 1 \longrightarrow_$$

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mPEG — OH

1. CI
$$\stackrel{\circ}{\longrightarrow}$$
 NO₂

2. 1-amino-2-propanol or -2-butanol

3. CH₃SO₂CI / TEA
4. Tr-SH / NaH
5. CH₃OCOSCI

mPEG — O $\stackrel{\circ}{\longrightarrow}$ N $\stackrel{\circ}{\longrightarrow}$ OCH₃

$$\stackrel{\circ}{\longrightarrow}$$
 OCH₃

$$\stackrel{\circ}{\longrightarrow}$$
 OH

$$\stackrel{\circ}{\longrightarrow}$$
 HIS $\stackrel{\circ}{\longrightarrow}$ OCH₃

$$\stackrel{\circ}{\longrightarrow}$$
 OH

$$\stackrel{\circ}{\longrightarrow}$$
 OH

$$\stackrel{\circ}{\longrightarrow}$$
 OCH₃

$$\stackrel{\circ}{\longrightarrow}$$
 OH

$$\stackrel{\longrightarrow$$

Fig. 4A

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$$\begin{array}{c|c}
 & O & \\
 & N & \\
 &$$

Fig. 4B

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$$H_{2}N \xrightarrow{R} OH \xrightarrow{1. H_{2}SO_{4}} \bigoplus_{H_{3}N} \bigoplus_{R} OSO_{3}^{\ominus} \xrightarrow{2. CS_{2}} \underbrace{NaOH} \qquad \begin{bmatrix} H \\ N \\ S \end{bmatrix} S \xrightarrow{S} S \xrightarrow{3. aq. HCl,} \bigoplus_{Reflux, 7 \text{ days}} \bigoplus_{H_{3}N} SH \\ R = CH_{3}, C_{2}H_{5}, C_{3}H_{7} \xrightarrow{4. CH_{3}OCOSCI} \\ MPEG - O \xrightarrow{N} \underset{R}{\overset{1}{\underset{N}{\bigvee}}} S \xrightarrow{S} OCH_{3} \xrightarrow{O} OH \xrightarrow{N} \underset{R}{\overset{1}{\underset{N}{\bigvee}}} S \xrightarrow{S} OCH_{3} \xrightarrow{N} OCH_{3} OCH_{3} \xrightarrow{N} OCH_{3} OCH_{3} \xrightarrow{N} OCH_{3} OCH_{$$

Fig. 5

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$$\begin{array}{c} \text{mpeg} - \text{o} \\ \text{N} \\ \text{H} \\ \text{CH}_{3} \\ \text{Cysteine / glutathione} \\ \text{(any thiol, R-SH)} \\ \end{array}$$

$$\begin{array}{c} \text{mpeg} - \text{o} \\ \text{N} \\ \text{H} \\ \text{CH}_{3} \\ \text{O} \\ \text{O} \\ \text{C}_{17}\text{H}_{35} \\ \text{C}_{17}\text{H}_{35} \\ \text{C}_{17}\text{H}_{35} \\ \text{O} \\ \text{O} \\ \text{O} \\ \text{C}_{17}\text{H}_{35} \\ \text{C}_{17}\text{H}_{35} \\ \text{O} \\ \text{O} \\ \text{O} \\ \text{O} \\ \text{C}_{17}\text{H}_{35} \\ \text{C}_{17}\text{H}_{35} \\ \text{O} \\ \text{O$$

Fig. 6B

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$$CH_{3}O-PEG-NH_{2}$$

$$CH_{3}O-PEG-NH_{1}$$

$$CH_{3}O-PEG-NH_{1}$$

$$CH_{3}O-PEG-NH_{1}$$

$$CH_{3}O-PEG-NH_{1}$$

$$CH_{3}O-PEG-NH_{1}$$

$$CH_{3}O-PEG-NH_{1}$$

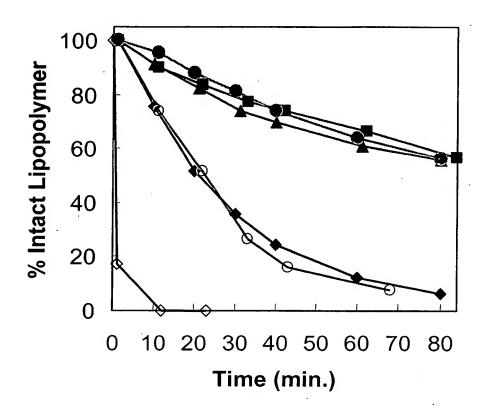
$$CH_{3}O-PEG-NH_{1}$$

$$CH_{3}O-PEG-NH_{2}$$

$$CH_{3}O$$

Fig. 6C

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- → mPEG2K-pDTB-DSPE
- → mPEG2K-oDTB-DSPE
- ---- mPEG2K-Me-pDTB-DSPE
- → mPEG2K-Me-oDTB-DSPE
- → mPEG2K-Et-pDTB-DSPE
- mPEG5K-Me-pDTB-DSPE

Fig. 7

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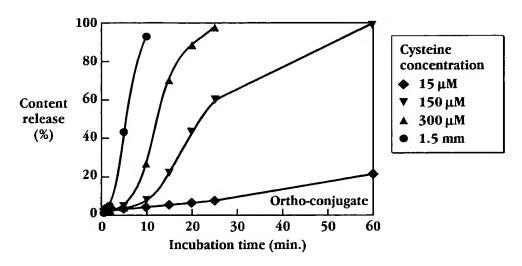


Fig. 8A

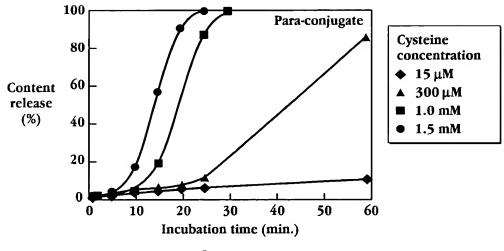
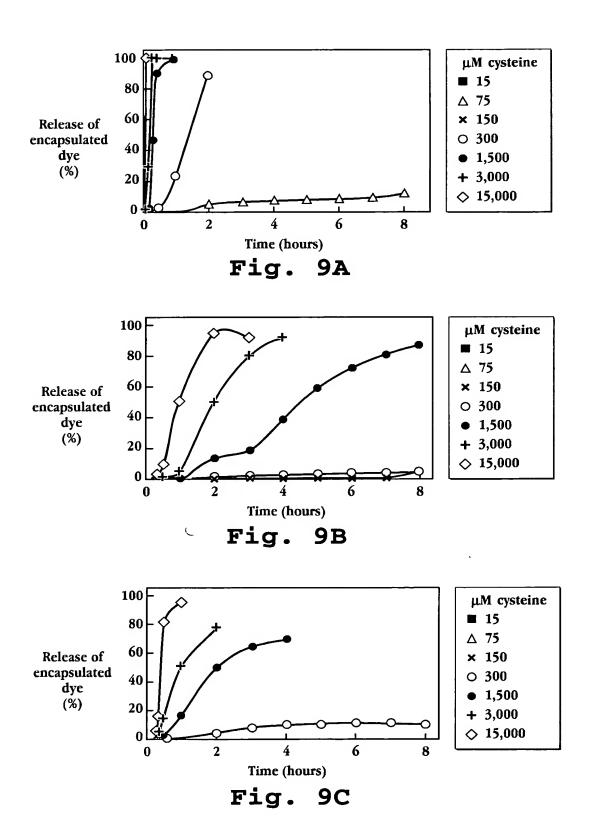


Fig. 8B

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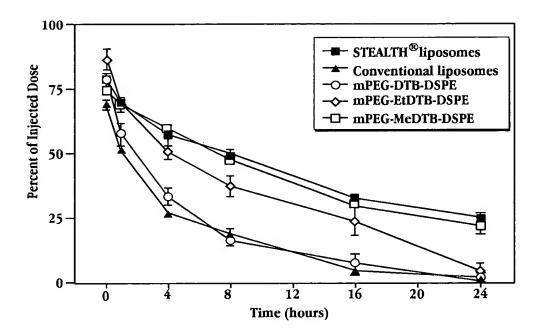


Fig. 10

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$$CH_{3} = 0 \longrightarrow_{n} 0 \longrightarrow_{N} S \longrightarrow_{S} 0 \longrightarrow_{N} O \longrightarrow_{NO_{2}} O$$

Fig. 11A

$$CH_{3} = O \longrightarrow_{n} O \longrightarrow_{H} S \longrightarrow_{S} S$$

$$Cys = SH$$

$$CH_{3} = O \longrightarrow_{n} O \longrightarrow_{H} S \longrightarrow_{R} S \longrightarrow_{S} Cys + S \longrightarrow_{H} CO_{2} + H_{2}N \longrightarrow_{Polypeptide} O$$

Fig. 11B

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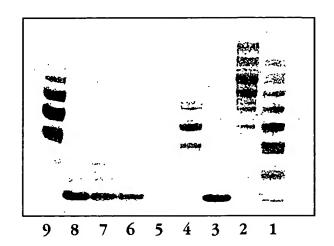


Fig. 12A

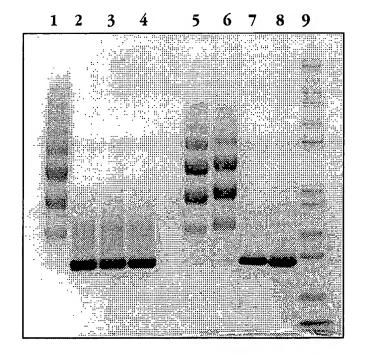


Fig. 12B

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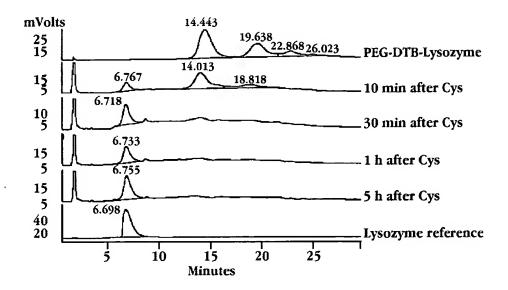


Fig. 13A

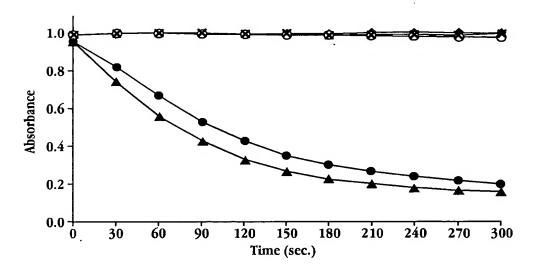


Fig. 13B

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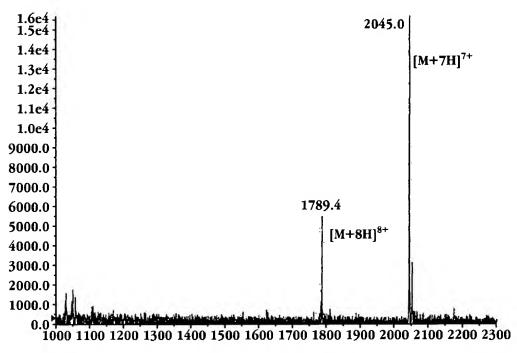


Fig. 14A

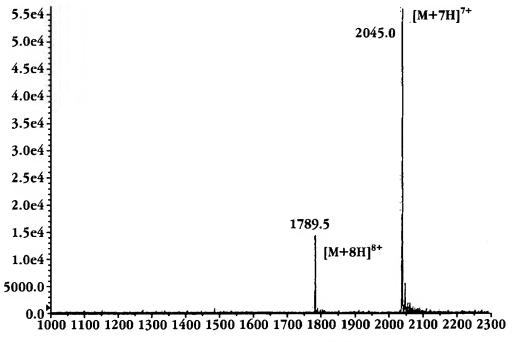


Fig. 14B

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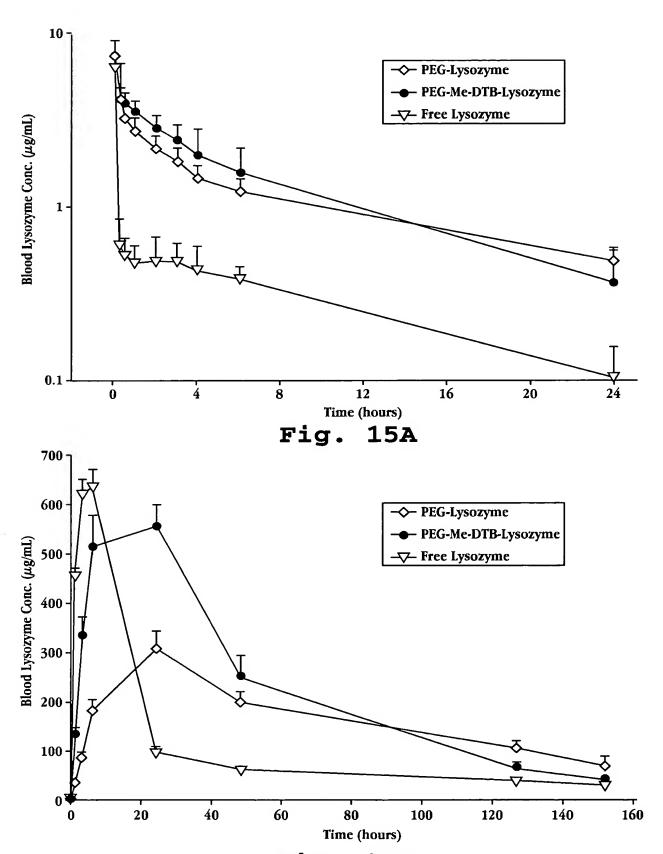


Fig. 15B

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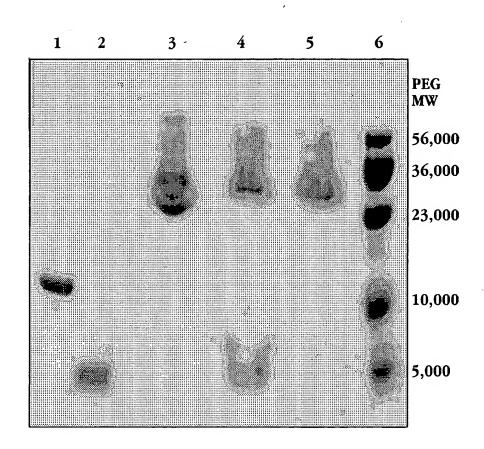


Fig. 16A

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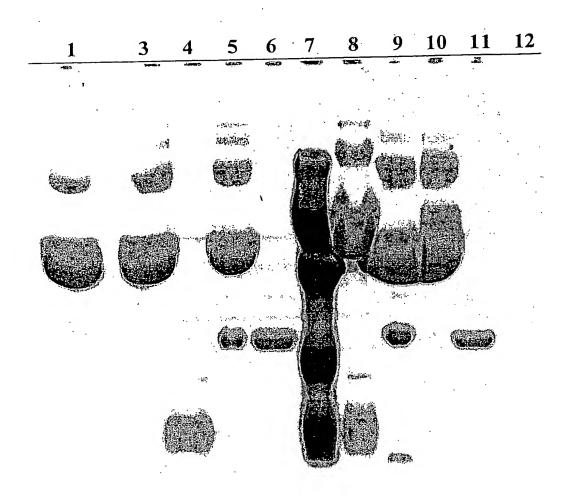
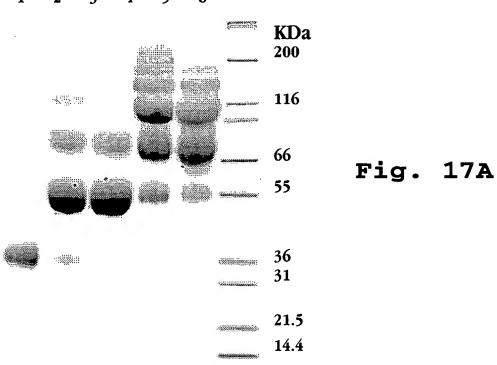


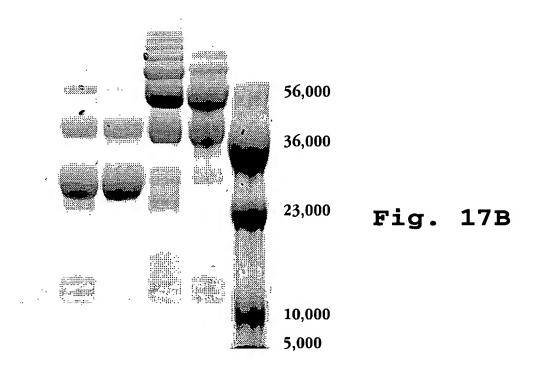
Fig. 16B

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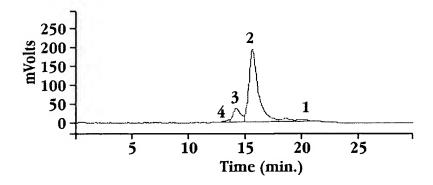


Fig. 18A

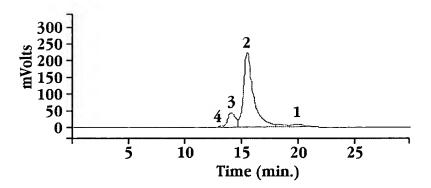


Fig. 18B

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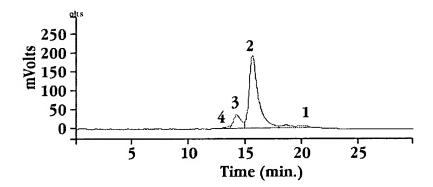


Fig. 18C

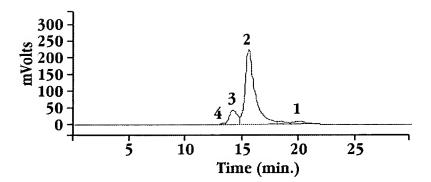


Fig. 18D

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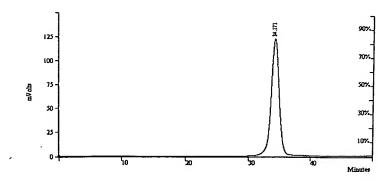


Fig. 19A

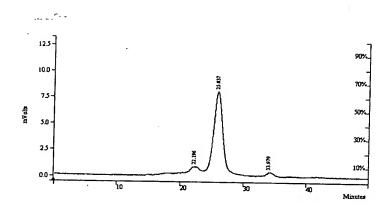


Fig. 19B

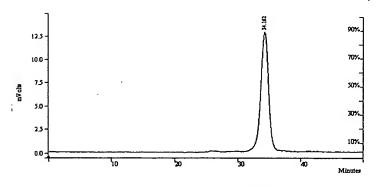


Fig. 19C

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Fig. 20A

Mitomycin C (MMC)

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5-Fluorouracil (5FU)

Fig. 20B

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Paclitaxel (Ac, acetyl; Bz, benzoyl; Ph, phenyl)

Fig. 20C

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Chlorambucil

Fig. 20D

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$$mPEG-O \xrightarrow{N} \underset{H}{\overset{O}{\bigvee}} SH + H_2N \xrightarrow{NO_2}$$

Fig. 21A

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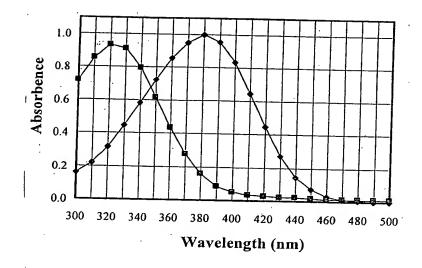


Fig. 21B

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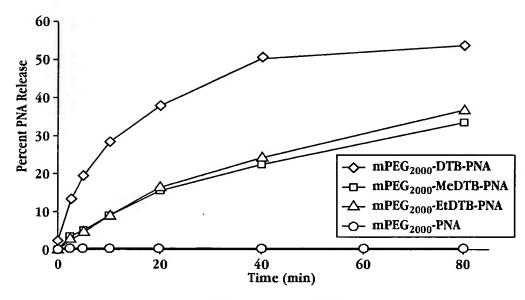


Fig. 22A

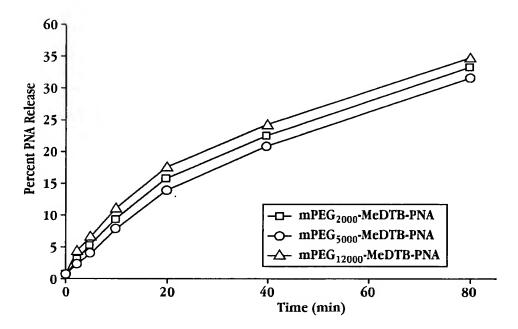


Fig. 22B